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Attorney Docket No. 13716
2058-181**REMARKS****I. Request To Withdraw Finality Of The Office Action.**

Applicants respectfully submit that the finality of Office Action dated September 22, 2004 is premature and request that the Examiner withdraw the finality of the Office Action.

Under United States Patent Office practice and procedure, final rejection is improper on a second or any subsequent action on the merits in any application if it includes a rejection based on newly cited art of *any claim* not amended by applicant in spite of the fact that other claims may have been amended to require newly cited art. *See*, MPEP 706.07(a).

In the present application, Claims 28 and 29 were not amended by Applicant. Claims 28 and 29 were originally presented in the Request for Continued Examination dated December 29, 2003 and were subsequently not amended prior to the Office Action dated September 22, 2004. The Office newly cited Hearn, M.T.W. "Methods in Enzymology", 1987, Vol 135, pages 102-117 in rejecting these claims in the Final Office Action. Accordingly, the finality of the Office Action dated September 22, 2004 is improper.

Applicants request that the Examiner withdraw the finality of the Office Action dated September 22, 2004 and regard this Response as a Response to a non-final Office Action.

II. Status Of The Claims.

With this Response and Amendment Claims 1-15, 18, 20-25, 27, 29, and 32-34 are pending. Claims 1, 12, 20, 27, 29, and 32-34 are amended. All pending claims are rejected under 35 U.S.C. § 103(a).

III. Claim Amendments.

The amendments to Claims 1, 12, 20, 27, 29, and 32-34 (a) do not add new matter or present new issues requiring further consideration or search. Further, as described below, the amended claims place the case in condition for allowance or in better condition for appeal. Entry of these amendments is respectfully requested.

Claims 1, 12, 20, 27 and 29.

Claims 1, 12, 20, 27, and 29 have been amended to add the phrase " . . . providing a solid support comprised of an organic polymer having at least one available amino group . . .".

This limitation was previously presented in now canceled Claim 30. Examples of solid

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supports comprised of organic polymers are described on page 6, lines 15-17 of the specification as natural and synthetic materials such as cellulose, agarose, polypropylene, polystyrene, polymethacrylate, and nylon. Each of these materials is an organic polymer, *i.e.*, a polymer with a backbone containing primarily carbon atoms, and the phrase "organic polymer" is an inherent characteristic of the described solid support materials. Further, solid supports comprised of an organic polymer with an available amino group are described in U.S. Pat. No. 5,112,736, incorporated by reference into the specification. Accordingly, new Claims 1, 12, 20, 27 and 29 do not add new matter or present new issues requiring further consideration or search.

Claims 32-34.

Claims 32-34 are amended so they are now dependent on Claim 1. Claims 32-34 are based on the specification, *See, e.g.*, pages 2-3; and 4-5 and do not add new matter or present new issues requiring further consideration or search.

IV. The Claimed Invention.

The invention is directed to a method for attaching biological molecules to a solid support in a two-step process. The present invention solves the problems of the prior art, which generally requires more than two steps, by requiring the combination of a solid support with an available amino group, and an activating group, which attaches both the solid support and the biological molecule. The advantages of the claimed invention over the prior art are that it is more efficient, economical, simpler and faster, with greater sensitivity.

For example, the present invention solves problems of the prior art, the acyl fluoride ("AcF") method of attachment disclosed in Milton, U.S. No. 6,143,833 by reducing the number of steps necessary to covalently attach a biological molecule to a solid support, and increasing the loading of biological molecules onto the solid support for synthesis and analyte detection. (*See, e.g.*, Specification, page 1).

V. The 35 USC § 103 Rejections.

Claims 1-4, 9-11, 18, 20-21, 25-31, 33, and 34 are rejected under 35 U.S.C. § 103(a) as unpatentable over Hearn ("Methods in Enzymology", 1987, Vol 135, pp. 102-117) and Stoloritz et al. (WO 87/06586) for the reasons stated in numbered paragraph 6 of the Office

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Action.

Claims 1-15, 18, and 20-36 are rejected under 35 U.S.C. § 103(a) as unpatentable over Hearn ("Methods in Enzymology", 1987, Vol 135, pages 102-117), Stolowitz et al. (WO 87/06586), Milton (US 6,146,833), Okamoto et al. (US 6,476,215), and Guo et al. (Nuc. Acids Res. 1994, pp. 5456-5465) for the reasons stated in numbered paragraph 8 of the Office Action.

Applicants respectfully traverse these rejection on the basis that (1) the Office has not established a *prima facie* case of obviousness; and (2) Milton teaches away from using "an organic polymer having at least one available amino group" to attach a biological molecule. Applicants respectfully request withdrawal of the rejection and allowance of Claims 1-15, 18, and 20-25, 27, 29, and 32-34 on the following basis.

A. The Office Has Not Established A Prima Facie Case Of Obviousness.

Each of the independent claims, Claims 1, 12, 20, 27, and 29 are each limited to "a solid support comprised of an organic polymer having at least one available amino group".

As admitted by the Office Hearn does not teach Applicant's claimed "organic polymer having at least one available amino group" (*See, e.g.*, Office Action, page 6). The Office looks to Stolowitz et al, Milton et al., Okamoto et al., and Guo et al. to remedy the deficiencies of Hearn. (Office Action, pages 9-12). However, Stolowitz et al., Okamoto et al., and Guo et al., also do not disclose Applicant's claimed "organic polymer having at least one available amino group", as these references disclose glass or silica as substrates, and thus do not remedy the deficiencies of Hearn.

1. There Is No Suggestion Or Motivation To Combine Hearn With Milton As The Proposed Combination of Hearn and Milton Changes The Principle Of Operation Of The References.

The Office states that "[i]t would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the CDI immobilization chemistry taught by Hearn and Stolowitz et al. in an array type format using a "printing method" to deliver the amine compound (e.g. oligonucleotides or peptides as taught by Milton, Guo and Okamoto because "immobilization" of biomolecules is required in each case (i.e., the references represent

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analogous art)." (Office Action, page 11).

Applicants respectfully submit that one of ordinary skill in the art would not be motivated to modify or combine Hearn and Milton because the proposed combination of Milton and Hearn changes the principle of operation of the references and the proposed combination would not result in an "immobilization" of biomolecules. Accordingly, the teachings of the references are not sufficient to render the claims *prima facie* obvious. MPEP § 2143.01.

Initially, Applicants would like to point out that the procedure for immobilizing biopolymers disclosed in Milton is a three-step process (*i.e.*, (1) derivatizing the aminated substrate to a carboxylated substrate; (2) treating the carboxylated substrate to form an acyl fluoride functionality; and (3) reacting the acyl fluoride functionality on the substrate with a biopolymer). In contrast, Applicants' claimed method is a two-step process where an activating compound is reacted with both an amino group on a solid support and a biological molecule.

Milton teaches immobilizing biopolymers on solid supports having acyl fluoride functionalities. As described throughout Milton, and shown in the scheme in Cols. 17-19 of Milton, aminated polypropylene is disclosed, among a myriad of other polymeric materials, as a starting material that is derivatized to have carboxyl functionalities. The carboxyl functionalities are then treated with a suitable reagent for forming an acyl fluoride functionality. The acyl fluoride functionality is then reacted with an amino derivatized biopolymer.

Following the teachings of Milton, and combining Milton with the teachings of Hearn, results in a substrate having an acyl fluoride functionality, not Applicants claimed "organic polymer having at least one available amino group". Reacting an acyl fluoride with the CDI described in Hearn would not result in attachment of the CDI and subsequent attachment of the biological molecule. Both the acyl fluoride and the CDI are acyl compounds which typically undergo nucleophilic substitution and neither of these compounds is reactive as a base (*i.e.*, a nucleophile). Accordingly, the modification changes the principle of operation of the references, *i.e.*, the proposed combination would not immobilize a biopolymer, and there is no

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suggestion or motivation to modify the references. Applicants request withdrawal of the rejection and allowance of all pending claims, Claims 1-15, 18, 20-25, 27, 29, and 32-34 on this basis.

B. Milton Teaches Away From Using “an organic polymer having at least one available amino group”.

The Office looks to Milton to remedy the deficiencies of Hearn. However, the references must be considered in their entirety. MPEP § 2141.02. Milton as a whole teaches the unsuitability of aminated polymer films for attaching biopolymers, and, in reference to derivatized polypropylene films, teaches that “there is a continuing need for improved material suitable for immobilizing biopolymers.” (Milton, col. 2, lines 5-27). Thus, Milton teaches away from “an organic polymer having at least one available amino group”, an element of all pending claims, there is no motivation to combine Hearn with Milton.

As detailed above, Milton teaches aminated polymers for use as starting materials only. Further, Milton teaches away from the combination with Hearn by teaching that underivatized aminated sites on the starting polymer should be *blocked* prior to reaction with a biopolymer. (Milton, col. 17, line 9, through col. 18, line 2). It is improper to combine references where the references teach away from their combination. MPEP § 2145(X)(D)(2). Accordingly, there is no suggestion in Milton that “an organic polymer having at least one amino group” is desirable for attaching a biological molecule.

Milton also teaches that prior art derivatized polypropylene films, glass slides, silicon wafers and polymer films are difficult to handle and require special handles or holders that are expensive to manipulate the solid support (Milton, col. 2, lines 5-27). Milton also teaches that “it is difficult to characterize and control the surface density of biopolymers synthesized or attached to glass slides and polypropylene films” and that “there is a need for improved materials suitable for immobilizing biopolymers”. (Milton, col. 2, lines 5-27). Milton then teaches that solid supports fabricated with acyl fluoride functionalities overcome the disadvantages of the prior art. (Milton, col. 3, lines 53-66).

Accordingly, one of skill in the art, considering Milton in its entirety, would not be motivated to select one of the myriad of starting materials disclosed in Milton, *e.g.*, an

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aminated polypropylene, and combine it with Hearn, as Milton describes the unsuitability of attaching biopolymers with this material. Applicants request withdrawal of the rejection and allowance of all pending claims, Claims 1-15, 18, 20-25, 27, 29, and 32-34 on this basis.

CONCLUSION

The Applicant believes that all pending claims are in condition for allowance and such action is earnestly requested. If the present amendments and remarks do not place the Application in condition for allowance, the Examiner is encouraged to contact the undersigned directly if there are any issues that can be resolved by telephone with the Applicants representative.

The Commissioner is authorized to charge the fee of \$790.00 for a Request for Continued Examination, and \$1,020.00 for a three-month extension to respond to the Final Office Action, to Deposit Account No. 19-2090. The Commissioner is further authorized to charge any other fees associated with this Response and Amendment to Deposit Account No. 19-2090.

Respectfully Submitted,
SHELDON & MAK PC

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By: 

Kristin C. Hübner, Ph.D.
Reg. No. 50,139

SHELDON & MAK PC
225 South Lake Avenue, 9th Floor
Pasadena, California 91101-3005

Telephone (626) 796-4000
Facsimile (626) 795-6321